

1 Claims

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3 1. A method for synthesising a given peptide or

4 its derivative which contains a proline

5 residue or a proline derivative, at proximity

6 to, or at, the C-terminal end of said peptide,

7 the method comprising the steps of:

8 a) synthesising on a first resin a C-

9 terminal portion of said peptide, or its

10 derivative, comprising at least three

11 successive amino acid residues or their

12 derivatives, by successive coupling of

13 selected amino acids, small peptides or

14 their derivatives, said first resin being

15 suitable for the formation of peptides

16 having a proline residue or a proline

17 derivative positioned at, or at proximity

18 of, the C-terminal end of said peptide;

19 b) cleaving the C-terminal portion thus

20 obtained from said first resin;

21 c) reattaching said C-terminal portion to a

22 second resin which is generally suitable

23 for the synthesis of peptides but is

24 unsuitable for the formation of peptides

25 having a proline residue or a proline

26 derivative positioned at, or at proximity

27 of, the C-terminal end of said peptide;

28 and

29 d) coupling selected amino acids, small

30 peptides or derivatives to the C-terminal

31 portion to obtain said given peptide.

1 2. The method of Claim 1 wherein said peptide is
2 a long peptide.

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4 3. The method of Claim 1 or 2 wherein said given
5 peptide is a chemokine having a proline
6 residue or a proline derivative at the C-
7 terminal or at proximity thereof.

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9 4. The method of any one of Claims 1 to 3,
10 wherein said first resin is chosen so that it
11 does not lead to the formation of cyclic
12 dipeptide and in particular diketopiperazine
13 compounds.

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15 5. The method of any one of Claims 1 or 4,
16 wherein said step a) and/or d) is achieved by
17 successive coupling of the predetermined amino
18 acid residues or derivatives.

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20 6. The method of any one of Claims 1 to 5,
21 wherein said first resin for the formation of
22 the C-terminal portion is the 2-chlorotriptyl
23 chloride resin.

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25 7. The method of any one of Claims 1 to 6,
26 wherein said second resin is a resin of the
27 type having benzyl ester linkers.

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29 8. The method of any one of Claims 1 to 7,
30 wherein said second resin is a Wang type
31 resin.

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1 9. The method of any one of Claims 1 to 8,
2 wherein said given peptide as up to 150 amino
3 acid residues.

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5 10. The method of any one of Claims 1 to 9,
6 wherein the cleaving step is achieved using a
7 mild acid treatment, for example 20%
8 trifluoroethanol in dichloromethane.

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10 11. The method of any one of Claims 1 to 10,
11 wherein the C-terminal portion is fully
12 protected so it can be attached directly onto
13 the second resin.

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